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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,665	03/11/2005	Christophe de Romeuf	065691-0388	7255

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,665	DE ROMEUF ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37 and 38* is/are pending in the application.

4a) Of the above claim(s) *37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/01/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's species election of a method for evaluating the effectiveness of a monoclonal or polyclonal antibody wherein the method comprises an antibody-dependent cellular cytotoxicity, filed 02/27/2007, is acknowledged.

It is noted that an election becomes fixed when the claims in an application have received an action on their merits by the Office. See MPEP 818.01.

Therefore, the restriction requirement, mailed 11/27/2006, is deemed proper and made FINAL.

Claims 1-36 have been canceled.
Claims 37 and 38 have been added and are pending.

Claim 37 has been withdrawn from further consideration by the Examiner, under 37 C.F.R. 1.142(b), as being drawn to nonelected invention.

Claim 38 is currently under consideration.

2. Applicant's amendment to the specification, filed 02/27/2007, is acknowledged and has been entered.

3. This Office Action will be in response to applicant's arguments, filed 02/27/2007.

The rejections of record can be found in the previous Office Action, mailed 11/30/2005.

4. Applicant's IDS, filed 03/01/2006, is acknowledged and has been considered.

5. Applicant's petition to correct inventorship under 37 C.F.R. 1.48(a), filed 03/03/2006, is acknowledged. The request for the deletion of an inventor in this nonprovisional application under 37 CFR 1.48(a) is deficient because: A statement, from Nicolas Bihoreau being added as an inventor that the error in inventorship occurred without deceptive intention on his part, has not been received.

6. Claim 38 is objected to because of the usage of parenthesis. It is suggested that the parentheses be deleted from the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 38 is indefinite in the recitation of "a method for evaluating the effectiveness of a monoclonal or polyclonal antibody" because the method does not clearly set forth method steps and there is an absence of a resolution step, which reads back on the preamble of the claimed methods. For example, the claim lacks a step that relates the ADCC assay and the measurement of IL-2 back to the preamble of the claim.

B) Claim 38 is indefinite in the recitation of "the effectiveness of a monoclonal or polyclonal antibody..." because the metes and bounds of the limitation are unclear and ambiguous. It is not clear as to what constitute "the effectiveness of a monoclonal or polyclonal antibody".

C) Claim 38 recites the limitation "IL-2" in 38(c). There is insufficient antecedent basis for this limitation in the claim. The claim recite "at least one cytokine" in 38(c), not "IL-2".

D) Claim 38 is indefinite in the recitation of "wherein the measurement of the amount of IL-2 is correlated with an ADCC type activity" because the metes and bounds of the phrase is ambiguous and unclear. It is not clear how the measurement of IL-2 correlates with ADCC. The phrase is not defined by the claims, the specification does not provide a standard form ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

E) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 38 is drawn to a method for evaluating the effectiveness of a monoclonal or polyclonal antibody by using CD16 expressing effector cells, performing an ADCC assay and measuring the amount of IL-2, wherein the amount of IL-2 correlates with ADCC.

The instant specification discloses antibodies made in host cells such as YB2/0 exhibit enhanced ADCC and the instant specification further discloses methods of measuring Fc-related function of antibodies, e.g. anti-Rh(D) antibody, by measuring effector cell activation by ADCC and cytokine releases (see page 4-5, in particular). The specification further discloses that the effector cells can be Jurkat transfected with CD16 (e.g. see page 4) and the amount of cytokine release (e.g. IL-2 release) by the Jurkat/CD16 cells correlates positively with ADCC of the antibody (e.g. see pages 14-16).

The specification as-filed does not enable one skilled in the art to practice the claimed invention without undue amount of experimentation. The instant specification does not provide sufficient enabling description of the claimed method for evaluating the effectiveness of a monoclonal or polyclonal antibody by using CD16 expressing effector cells, performing an ADCC assay and measuring the amount of IL-2, wherein the amount of IL-2 correlates with ADCC.

The instant specification appears to evaluate only the ADCC effect, which is related to the Fc region of an antibody. The specification does not appear to disclose other well-known aspects related to the effectiveness of an antibody such as antigen-specificity.

Further, the specification discloses that effector cell can be Jurkat transfected with CD16. However, the specification does not provide sufficient guidance regarding how to perform an ADCC assay using Jurkat transfected with CD16 without target cells and how to correlate the amount of IL-2 produced by said effector cells with the ADCC. It appears that the instant specification discloses, when testing anti-Rh(D) antibody, that the higher the amount of IL-2 released by Jurkat/CD16 cell, the stronger ADCC observed (e.g. see Example 2 on page 14-16).

However, the state of the art recognized that both activating and inhibitory FcγR are involved in antibody effector function mediated by the Fc region of an antibody. For example, Siberl et al. (Clinical Immunology 2006 118:170-179) teach that anti-Rh(D) antibody prevents all-immunization by engaging both the activating FcγR and the inhibitory FcγRIIB1; anti-Rh(D) antibody made using host cells YB2/0 exhibits the best ability to trigger ADCC yet induces strong FcγRIIB-mediated inhibition of IL-2 production; this feature of inhibiting IL-2 production can be used to select candidate therapeutic monoclonal anti-Rh(D) antibody (see entire document, particularly Discussion on pages 177-179).

The reference teaches that inhibiting IL-2 production correlates with strong ADCC effect; this appears to be opposite of what has been disclosed in the instant specification. Given that it is not clear how the measurement of IL-2 is correlated with an ADCC as claimed, one skilled in the art would not be enabled to make and use the claimed method of evaluating the effectiveness of a monoclonal or polyclonal antibody.

Consequently, the experimentation left to those skilled in the art to determine how to make and use the claimed *method of evaluating the effectiveness of a monoclonal or polyclonal antibody comprising bringing CD16 expressing effector cells into contact with said antibody, measuring the amount of IL-2 produced by the effector cell, performing ADCC and correlate the amount of IL-2 with ADCC* is extensive and undue.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a *Written Description*, New Matter rejection.

The phrase "the antibody being activated by the antigen, and the antigen being different from the CD16" is not supported by the original disclosure or claim as filed.

Applicant's amendment, filed 02/27/2007, has not directed to support to the new claims in the instant specification and has not asserted that no new matter has been added.

The specification as filed does not provide sufficient written description of the above-mentioned "limitations". The specification does not provide sufficient support for "the antibody being activated by the antigen, and the antigen being different from the CD16". The specification only discloses antibodies, specific for antigens such as CD20, made in host cells such as YB2/0 (e.g. see Examples on pages 13-20 of the instant specification). Therefore, the claims represent a departure from the specification and claims originally filed.

Further, the specification does not have sufficient support for "the antigen being different from the CD16". The instant claim now recites limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed.

Furthermore, the recitation of "the antigen being different from the CD16" appears to be a negative limitation, Adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitation does, in fact, introduce new concepts. Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli, 231 USPQ 393 (Bd. App.1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984).

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Pullyblank et al. (British Journal of Cancer 1995. 72:601-606) (see entire document).

Pullyblank et al. teach a method for evaluating the effector function (e.g perfroming ADCC) of monoclonal antibodies and cytokine release(e.g IL-1 and TNF-α) from effector cells such as monocytes (see entire document, particularly Material and Methods on page 601-602). Further, Pullyblank et al. teach the cytokines released correlates with ADCC mediated tumor lysis (e.g. see Discussion on pages 604-605).

Therefore, the reference teachings anticipate the claimed invention.

13. Conclusion: no claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Crowder, Ph.D.
Patent Examiner
May 15, 2007

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TC 1600
5/17/07
5/17/07